

**What is claimed is:**

1. A peptide of formula I

$N_1DFYHSKRRLIFN_2$  (formula I) (SEQ ID No. 4),

comprising the motif XLXF,

wherein  $N_1$  and  $N_2$  are independently a natural or non-natural amino acid or nothing;

or the peptide of formula I having up to 8 amino acid residues deleted from the N-terminal end; and variants thereof wherein at least one amino acid residue is replaced by an alternative natural or non-natural replacement amino acid residue, with the proviso that the motif XLXF is retained, wherein X refers to any natural or unnatural amino acid.

2. A peptide according to claim 1, wherein  $N_1$  and  $N_2$  are independently selected from nothing and the polar residues C, N, Q, S, T and Y.
3. A peptide according to claim 2, wherein  $N_1$  is a natural or unnatural amino acid.
4. A peptide according to claim 3, wherein  $N_1$  is threonine.
5. A peptide according to claim 2, wherein  $N_2$  is a natural or unnatural amino acid.
6. A peptide according to claim 3, wherein  $N_1$  is serine.

7. A peptide according to claim 1, wherein up to 6 amino acid residues are deleted from the N-terminal end of the peptide of formula I.
8. A peptide according to claim 7, wherein from 3-5 amino acid residues are deleted from the N-terminal end of the peptide of formula I.
9. A peptide according to claim 8, wherein 4 amino acid residues are deleted from the N-terminal end of the peptide of formula I.
10. A peptide according to claim 7, wherein  $N_2$  is a natural or unnatural amino acid.
11. A peptide according to claim 10, wherein  $N_2$  is serine.
12. A peptide according to claim 1, wherein 7 or 8 amino acid residues are deleted from the N-terminal end of the peptide of formula I.
13. A peptide of formula

DFYHSKRRLIF (SEQ ID No. 1),

comprising the motif XLXF,

or such a peptide

- (i) bearing a further amino acid residue at either end; and,
- (ii) having up to 7 amino acid residues deleted from the N-terminal end;

and variants thereof wherein at least one amino acid residue is replaced by an alternative natural or unnatural replacement amino acid residue, with the proviso that the motif XLXF is retained, wherein the peptide of SEQ ID No. 1 is modified by at least one of; deletion, addition or substitution of one or more amino acid residues, or by substitution of one or more natural amino acid residues by the corresponding D-stereomer or by a non-natural amino acid residue, chemical derivatives of the peptides, cyclic peptides derived from the peptides or from the peptide derivatives, dual peptides, multimers of the peptides and any of said peptides in the D-stereomer form, or the order of the final two residues at the C-terminal end are reversed.

14. A variant according to claim 13, wherein the serine residue corresponding to p21(153Ser), is replaced by an alanine residue.

15. A peptide according to claim 13, selected from;

DFYHSKRRLIFS

TDFYHSKRRLIF,

AFYHSKRRLIFS,

DAYHSKRRLIFS,

DFAHSKRRLIFS,

DFYASKRRLIFS,

DFYHAKRRLIFS,

DFYHSARRLIFS,

DFYHSKRRLIFS,

DFYHSKRRLAFS,

DFYHSKRRLIFA,

FYHSKRRLIFS,

YHSKRRLIFS,

HSKRRLIFS,

DFYHSKRRLIF,

FYHSKRRLIF

YHSKRRLIF

HSKRRLIF,

SKRRLIF,

KRRLIF,

H- Arg- Leu- Ile- Phe -NH2

H- Arg- Arg- Leu- Ile- Phe -NH2

H- Lys- Arg- Arg- Leu- Ile- Phe -NH2

H- Ala- Lys- Arg- Arg- Leu- Ile- Phe -NH2

H- His- Ala- Lys- Arg- Arg- Leu- Ile- Phe -NH<sub>2</sub>

H- Asn- Leu- Phe- Gly -NH<sub>2</sub>

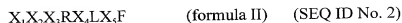
H- Arg- Asn- Leu- Phe- Gly -NH<sub>2</sub>

H- Abu- Arg- Asn- Leu- Phe- Gly -NH<sub>2</sub>

H- Ala- Abu- Arg- Asn- Leu- Phe- Gly -NH<sub>2</sub> and

H- Ser- Ala- Abu- Arg- Asn- Leu- Phe- Gly -NH<sub>2</sub>

16. A peptide of formula II;



wherein X<sub>1</sub>, X<sub>3</sub>, X<sub>4</sub> and X<sub>5</sub> may be any amino acid and X<sub>2</sub> is serine or alanine; and variants thereof.

17. A peptide according to claim 16, wherein X<sub>3</sub> is selected from isoleucine and glycine.

18. A peptide according to claim 16, wherein X<sub>1</sub> and X<sub>4</sub> are both basic amino acid residues and X<sub>3</sub> is a basic or polar residue.

19. A peptide according to claim 18, wherein X<sub>1</sub> is histidine and X<sub>4</sub> is arginine, and X<sub>3</sub> is lysine or cysteine.

20. A peptide of formula;



(SEQ ID No. 2)

wherein  $X_1$ ,  $X_3$ ,  $X_4$  and  $X_5$  may be any amino acid and  $X_2$  is serine or alanine; and variants thereof, wherein the peptide is modified by at least one of a deletion, addition or substitution of one or more amino acid residues, or by substitution of one or more natural amino acid residues by the corresponding D-stereomer or by a non-natural amino acid residue, chemical derivatives of the peptides, cyclic peptides derived from the peptides or from the peptide derivatives, dual peptides, multimers of the peptides and any of said peptides in the D-stereomer form, or the order of the final two residues at the C-terminal end are reversed.

21. A peptide of formula;



(SEQ ID No. 2)

wherein  $X_1$ ,  $X_3$ ,  $X_4$  and  $X_5$  may be any amino acid and  $X_2$  is serine or alanine; and variants thereof, wherein:

- (a)  $X_1$  is deleted or is any amino acid,
- (b)  $X_2$  is serine or alanine or a straight or branched chain amino acid,
- (c)  $X_3$  is a basic amino acid or straight chain aliphatic amino acid,
- (d) R is unchanged or conservatively substituted (by basic amino acids),
- (e)  $X_4$  is any amino acid that is capable of providing at least one site for participating in hydrogen bonding,
- (f) L is unchanged or conservatively substituted,
- (g)  $X_5$  is any amino acid, or

- (h) F is unchanged or substituted by any aromatic amino acid.

22. A peptide of formula;



wherein

- (a)  $X_1$  is histidine, deleted or replaced by a natural or unnatural amino acid residue such as alanine, 3-pyridylalanine (Pya), 2-thienylalanine (Thi), homoserine (Hse), phenylalanine, or diaminobutyric acid (Dab),
- (b)  $X_2$  is alanine or an alternative natural or unnatural amino acid residue having a smaller or slightly larger aromatic or aliphatic side chain, such as glycine, aminobutyric acid (Abu), norvaline (Nva), t-butylglycine (Bug), valine, isoleucine, phenylglycine (Phg) or phenylalanine,
- (c)  $X_3$  is lysine or either a basic residue such as arginine or an uncharged natural or unnatural amino acid residue, such as norleucine (Nle), aminobutyric acid (Abu) or leucine,
- (d) arginine is replaced by either a basic residue such as lysine or an uncharged natural or unnatural amino acid residue, such as citrulline (Cit), homoserine, histidine, norleucine (Nle) or glutamine,
- (e)  $X_4$  is arginine or a natural or unnatural amino acid residue, such as asparagine, proline, serine, aminoisobutyric acid (Aib) or sarcosine (Sar), or an amino acid residue capable of forming a cyclic linkage such as lysine or ornithine,
- (f) leucine is replaced with a natural or unnatural amino acid residue having a slightly larger aromatic or aliphatic side chain, such as norleucine, norvaline, cyclohexylalanine (Cha), phenylalanine or 1-naphthylalanine (1Nal),

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- (g) X<sub>5</sub> is isoleucine or an alternative natural or unnatural amino acid residue having a slightly larger aromatic or aliphatic side chain, such as norleucine, norvaline, cyclohexylalanine (Cha), phenylalanine or 1-naphthylalanine (1Nal),
- (h) phenylalanine is replaced with a natural or unnatural amino acid such as leucine, cyclohexylalanine (Cha), homophenylalanine (Hof), tyrosine, para-fluorophenylalanine (pFPhe), meta-fluorophenylalanine (mFPhe), trptophan, 1-naphthylalanine (1Nal), 2-naphthylalanine (2Nal), biphenylalanine (Bip) or (Tic),
- (i) X<sub>5</sub> and the terminal phenylalanine residue are reversed, or
- (j) the peptide is in cyclic form by the formation of a linkage between the side chain of X<sub>4</sub> and the C-terminus residue.

23. A peptide according to claim 16, wherein X<sub>2</sub> is alanine.

24. A peptide according to claim 16, wherein X<sub>5</sub> is isoleucine.

25. A peptide according to claim 20, selected from the group consisting of:

H S K R R L I F,

H A K R R L I F,

H S K R R L F G,

H A K R R L F G,

K A C R R L F G,

K A C R R L I F,

	X1	X2	X3	R	X4	L	X5	F
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe -NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe -NH <sub>2</sub>
	H-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe -NH <sub>2</sub>



H-	Pya-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	Thi-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	Hse-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	Phe-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	Dab-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Gly-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Abu-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Nva-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Bug-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Val-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ile-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Phg-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Phe-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Ala-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Nle-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Abu-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Leu-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Arg-	Arg-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Ala-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Cit-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Hse-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	His-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Nle-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Gln-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Lys-	Arg-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Ala-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Asn-	Leu-	Ile-	Phe	-NH2

H-	His-	Ala-	Lys-	Arg-	Pro-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Ser-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Aib-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Sar-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Cit-	Leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Ala-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	leu-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Ile-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Val-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Nle-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Nva-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Cha-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Phe-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	lNap-	Ile-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ala-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Leu-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Val-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Nle-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Nva-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Cha-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Phe-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	lNap-	Phe	-NH2
	H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Phe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Leu	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Cha	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Hof	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Tyr	-NH2

H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	pFPhe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	mFPhe	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Trp	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	1Nap	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	2Nap	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Lys	-NH2
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Tic	-NH2
H-	His	Ala	Lys	Arg	Arg	Leu	Ile	L-Pse	OH
H-	His	Ala	Lys	Arg	Arg	Leu	Ile	D-Pse	OH
H-	His	Ser	Lys	Arg	Arg	Leu	Ile	L-Pse	OH
H-	His	Ser	Lys	Arg	Arg	Leu	Ile	D-Pse	OH
H-	His	Ala	Lys	Arg	Arg	Leu	Ile	L-Psa	OH
H-	His	Ala	Lys	Arg	Arg	Leu	Ile	D-Psa	OH
H-	His	Ser	Lys	Arg	Arg	Leu	Ile	L-Psa	OH
H-	His	Ser	Lys	Arg	Arg	Leu	Ile	D-Psa	OH
H-	His	Ala	Lys	Arg	Arg	Leu	Ile	Dhp	OH
H-	His	Ser	Lys	Arg	Arg	Leu	Ile	Dhp	OH
H-	His	Ala	Lys	Arg	Arg	Leu	Ile	Pheol	
H-	His	Ser	Lys	Arg	Arg	Leu	Ile	Pheol	
H-	Ala-	Ala-	Abu-	Arg-	Arg-	Leu-	Ile-	pFPhe	-NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	pFPhe	-NH2
H-	Ala-	Ala-	Lys-	Arg-	Cit-	Leu-	Ile-	pFPhe	-NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ala-	pFPhe	-NH2
H-	Ala-	Ala-	Abu-	Arg-	Ser-	Leu-	Ile-	pFPhe	-NH2
H-	Ala-	Ala-	Lys-	Gln-	Arg-	Leu-	Ile-	pFPhe	-NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	pFPhe	-NH2
H-	Gly-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	pFPhe	-NH2

H-	Ala-	Ala-	Lys-	hArg-	Arg-	Leu-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Ser-	Arg-	Leu-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Hse-	Arg-	Leu-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Lys-	Leu-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Orn-	Leu-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Gln-	Leu-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Hse-	Leu-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Thr-	Leu-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Nva-	Leu-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Phg-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Met-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Ala-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Hof-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	hLeu-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	alle-	Ile-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Gly-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	βAla	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Phg-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Aib-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Sar-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Pro-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Bug-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ser-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Asp-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Asn-	pFPhe -NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	pFPhe- Phe	-NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	diCIPhe Phe	-NH2

H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	pClPhe-	Phe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	mClPhe	Phe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	oClPhe-	Phe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	pIPhe-	Phe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	TyrMe-	Phe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Thi-	Phe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Pyra-	Phe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	diClPhe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	pClPhe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	mClPhe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	oClPhe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phg	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	TyrMe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Thi	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Pyra	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Inc	-NH <sub>2</sub>

and the cyclic peptides:

5,8-cyclo-[H-His-Ala-Lys-Arg-Lys-Leu-Phe-Gly]

5,8-cyclo-[H-His-Ala-Lys-Arg-Orn-Leu-Phe-Gly]

26. A peptide of the formula III or IV;

H<sup>+</sup>X<sub>2</sub>K<sup>+</sup>R<sub>1</sub>R<sub>2</sub>L<sup>+</sup>X<sub>3</sub>F (formula III) (SEQ ID No.     ) or H<sup>+</sup>X<sub>2</sub>K<sup>+</sup>R<sub>1</sub>R<sub>2</sub>L<sup>+</sup>FX<sub>3</sub> (formula IV)  
(SEQ ID No.     )

or a variant thereof, wherein

H' is nothing, His, D-His, Ala, Thi, Hse, Phe, or Dab;

X<sub>2</sub> is Ala, Ser, Abu, Val;

K' is Lys, Arg, or Abu;

R<sub>1</sub> is Arg, Lys, or Gln; and

R<sub>2</sub> is Arg, forms a cyclic peptide with the C-terminal residue, Ser, or Cit;

L' is Leu or Ile;

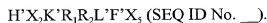
X<sub>3</sub> is Ile, Leu, Gly, or Ala; and

F' is Phe, para-fluoroPhe, meta-fluoroPhe, L-Psa, 2-Nap,Dhp, or D-Psa.

27. A peptide according to claim 26, wherein X<sub>2</sub> is alanine.

28. A peptide according to claim 26, wherein X<sub>3</sub> isoleucine.

29. A peptide according to claim 26 of the formula IV



30. The peptide of claim 26, wherein the peptide is in a cyclic form by virtue of a linkage between the C-terminal residue and the residue 3 upstream to it.

31. A peptide according to claim 30, wherein  $X_2$  is Ala and  $X_5$  is Ile.
32. A peptide according to claim 26, wherein F' is para-fluoro-Phe and H' is Ala or nothing.
33. The peptide of claim 26, wherein K' is Abu;  $R_1$  is Gln;  $R_2$  is Cit or Ser; and  $X_5$  is Ala.
34. A peptide according to claim 26 selected from the group consisting of:

H-	his-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH <sub>2</sub>
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH <sub>2</sub>
	H-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH <sub>2</sub>
H-	Thi-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH <sub>2</sub>
H-	Hse-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH <sub>2</sub>
H-	Phe-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH <sub>2</sub>
H-	Dab-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH <sub>2</sub>
H-	His-	Abu-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH <sub>2</sub>
H-	His-	Val-	Lys-	Arg-	Arg-	Leu-	Ile-	Phe	-NH <sub>2</sub>
H-	His-	Ala-	Arg-	Arg-	Arg-	Leu-	Ile-	Phe	-NH <sub>2</sub>
H-	His-	Ala-	Lys-	Arg-	Arg-	Ile-	Ile-	Phe	-NH <sub>2</sub>
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Leu-	Phe	-NH <sub>2</sub>
H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	pFPhe	-NH <sub>2</sub>

H-	His-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	2Nap	-NH2
H-	His	Ala	Lys	Arg	Arg	Leu	Ile	D-Psa	OH
H-	His	Ser	Lys	Arg	Arg	Leu	Ile	Dhp	OH
H-	Ala-	Ala-	Abu-	Arg-	Arg-	Leu-	Ile-	pFPhe	-NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	pFPhe	-NH2
H-	Ala-	Ala-	Lys-	Arg-	Cit-	Leu-	Ile-	pFPhe	-NH2
H-	Ala-	Ala-	Lys-	Arg-	Arg-	Leu-	Ala-	pFPhe	-NH2
H-	Ala-	Ala-	Abu-	Arg-	Ser-	Leu-	Ile-	pFPhe	-NH2
H-	Ala-	Ala-	Lys-	Gln-	Arg-	Leu-	Ile-	pFPhe	-NH2
	H-	Ala-	Lys-	Arg-	Arg-	Leu-	Ile-	pFPhe	-NH2

35. An assay for identifying candidate substances capable of binding to a cyclin associated with a G1 control CDK enzyme and/or inhibition of said enzyme, comprising;

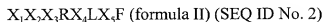
(a) bringing into contact i) a p21 derived peptide as defined in claim 1, ii) said cyclin or portion thereof or cyclin groove, iii) said CDK or portion thereof and iv) said candidate substance, under conditions wherein, in the absence of the candidate substance being an inhibitor of the cyclin/CDK interaction, the p21 derived peptide would bind to said cyclin or portion thereof or cyclin groove, and

(b) monitoring any change in the expected binding of the p21 derived peptide and the cyclin or portion thereof or cyclin groove.

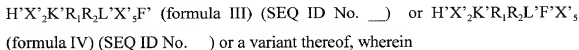
36. An assay for the identification of compounds that interact with a cyclin or a cyclin when complexed with the physiologically relevant CDK, comprising;



(a) incubating a candidate compound and peptide of formula I;



wherein  $X_1$ ,  $X_3$ ,  $X_4$  and  $X_5$  may be any amino acid and  $X_2$  is serine or alanine; and variants thereof or a peptide of the formula III or IV:



$H'$  is His, nothing, D-His, Ala, Thi, Hse, Phe, or Dab;

$X'_2$  is Ala, Ser, Abu, Val;

$K'$  is Lys, Arg, or Abu;

$R_1$  is Arg, Lys, or Gln; and

$R_2$  is Arg, forms a cyclic peptide with the C-terminal residue, Ser, or Cit;

$L'$  is Leu or Ile;

$X'_3$  is Ile, Leu, Gly, or Ala;

$F'$  is Phe, para-fluoroPhe, meta-fluoroPhe, L-Psa, 2-Nap,Dhp, or D-Psa.

and a cyclin or cyclin/CDK complex;

(b) detecting binding of either the candidate compound or the peptide of formula II or III with cyclin.

37. An assay for candidate compounds that interact with a cyclin by virtue of forming associations with at least two of the amino acids corresponding to the cyclin A amino acids L253, I206 and R211.

38. An assay according to claim 37, wherein the candidate compound additionally forms associations with at least one of the amino acids corresponding to the cyclin A amino acids E223, E224, D284, D283, L253, I206 and R211.

39. An assay according to claim 37, wherein the candidate additionally forms associations with at least one of the amino acids corresponding to the cyclin A amino acids W217, V219, V221, S408, E411, Y225, I213, L214, G257, R250, Q254, T207 and L214.

40. An assay according to claim 37, wherein the candidate compound additionally forms associations with at least one of the amino acids corresponding to the cyclin A amino acids G222, Y225, I281, E223, E220, V279, A212, V215, L218, Q406, S408, M210, L253, L218, I239, V256 and M200.

41. An assay according to claim 35, wherein the cyclin is selected from cyclin A, cyclin E or cyclin D.

42. An assay according to claim 41 wherein the cyclin is cyclin A.

43. An assay according to claim 35, comprising use of a three dimensional model of a cyclin and a candidate compound.

44. An assay according to claim 35, wherein at least one of the assay components is

bound to a solid phase.

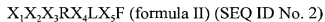
45. An assay according to claim 44, wherein the p21 derived peptide is labeled such as to emit a signal when bound to said cyclin.

46. An assay according to claim 44, wherein the cyclin is labeled such as to emit a signal when bound to the p21 derived peptide.

47. An assay according to claim 45, wherein one of the assay components is labeled with a fluorescence emitter and the signal is detected using fluorescence polarization techniques.

48. A method of using a cyclin in a drug screening assay comprising:

- (a) selecting a candidate compound by performing rational drug design with a three-dimensional model of said cyclin, wherein said selecting is performed in conjunction with computer modeling;
- (b) contacting the candidate compound with the cyclin; and
- (c) detecting the binding affinity of the candidate compound for the cyclin groove; wherein a potential drug is selected on the basis of its having a greater affinity for the cyclin groove than that of a peptide of formula II;



wherein  $X_1$ ,  $X_3$ ,  $X_4$  and  $X_5$  may be any amino acid and  $X_2$  is serine or alanine; and variants thereof or a peptide of formula III or IV:



(formula IV) (SEQ ID No. \_\_) or a variant thereof, wherein

H' is His, nothing, D-His, Ala, Thi, Hse, Phe, or Dab;

X<sub>2</sub>' is Ala, Ser, Abu, Val;

K' is Lys, Arg, or Abu;

R<sub>1</sub> is Arg, Lys, or Gln; and

R<sub>2</sub> is Arg, forms a cyclic peptide with the C-terminal residue, Ser, or Cit;

L' is Leu or Ile;

X<sub>3</sub>' is Ile, Leu, Gly, or Ala;

F' is Phe, para-fluoroPhe, meta-fluoroPhe, L-Psa, 2-Nap,Dhp, or D-Psa.

49. A method of using a cyclin in a drug screening assay comprising:

- (a) selecting a candidate compound by performing rational drug design with a three-dimensional model of said cyclin, wherein said selecting is performed in conjunction with computer modeling;
- (b) contacting the candidate compound with the cyclin; and
- (c) detecting whether said the candidate compound forms associations with at least the amino acids corresponding to the cyclin A amino acids L253, I206 and R211.

50. A method according to claim 49, further comprising detection of whether the candidate compound additionally forms associations with at least one of the amino acids corresponding to the cyclin A amino acids E223, E224, D284, D283, L253, I206 and R211.

51. A method according to claim 50, further comprising detection of whether the candidate compound additionally forms associations with at least one of the amino acids corresponding to the cyclin A amino acids W217, V219, V221, S408, E411, Y225, I213, L214, G257, R250, Q254, T207 and L214.

52. A method according to claim 50, further comprising detection of whether the candidate compound additionally forms associations with at least one of the amino acids corresponding to the cyclin A amino acids G222, Y225, I281, E223, E220, V279, A212, V215, L218, Q406, S408, M210, L253, L218, I239, V256 and M200.

53. An assay for identifying candidate substances capable of inhibiting CDK in a cell, comprising;

(a) contacting a cell comprising a cyclin or portion thereof or cyclin groove, and a CDK or portion thereof, with a candidate substance under conditions where, in the absence of the candidate substance, the cyclin or portion thereof or cyclin groove and CDK or portion thereof would interact, and

(b) monitoring any change in the activity of the CDK or portion thereof, wherein inhibition of CDK activity is indicated by one or more of: G0 and/o G1/S cell cycle arrest; cell cycle-related apoptosis; suppression of E2F transcription factor activity; hypophosphorylation of cellular pRb; and in vitro anti-proliferative effects.

54. Use of a peptide defined in claim 1 in the preparation of a medicament for use in (a) inhibition of CDK2 or (b) in the treatment of proliferative disorders such as cancers and leukaemias where inhibition of CDK2 would be beneficial.